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Article type : Systematic Review

A Systematic Review of CT Chest in COVID-19 Diagnosis and its Potential Application in a Surgical Setting

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Funding/Financial Support

This work did not receive any financial support or funding

COI/Disclosures

Dr. Heniford has been awarded education grants and speaker honoraria from W.L. Gore and Allergan. Dr. Augenstein has received honoraria for speaking for Medtronic, Allergan, Intuitive, Acelity, and W.L. Gore. All conflicts of interest are outside of the scope of the submitted work. Dr. Shao, Dr. Ayuso, Dr. Deerenberg, and Dr. Elhage have no potential conflicts or disclosures.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/CODI.15252

Ethical Statement

Compliance with all ethical standards

Word Count: 3037

ABSTRACT

Aim

To investigate the sensitivity and utility of computed tomography (CT) of the chest in diagnosing active Coronavirus 2019 (COVID-19) infection, and its potential application to the surgical setting.

Methods

A literature review was conducted using Google Scholar® and MEDLINE®/PubMed® to identify current available evidence regarding the sensitivity of CT chest in comparison to RT-PCR for diagnosis of COVID-19 positive patients. GRADE criteria and the QUADAS 2 tool was used to assess the level of evidence.

Results

A total of 20 articles were identified that addressed the question of sensitivity of CT for diagnosis of COVID-19 positive symptomatic and asymptomatic patients. Overall sensitivity of CT scan ranged from 57%-100% for symptomatic and 46%-100% for asymptomatic COVID-19 patients, while that of RT-PCR ranged from 39%-89%. CT chest was a better diagnostic modality and capable of detecting active infection earlier in the time course of infection than RT-PCR in symptomatic patients. In asymptomatic patients, disease prevalence seems to play a role in the positive predictive value. Minimal evidence exists regarding the sensitivity of CT in patients who are asymptomatic.

Conclusions

In surgical patients, CT Chest should be considered as an important adjunct for detection of COVID-19 infection in patients who are symptomatic with negative RT-PCR prior to any operation. For surgical patients who are asymptomatic, there is insufficient evidence to recommend routine preoperative CT Chest for COVID-19 screening.

What does this add to the literature?

Utilization of CT chest in diagnosing and screening symptomatic and asymptomatic presurgical patients is poorly defined. This systematic review examines the evidence for obtaining CT chest for symptomatic RT-PCR negative patients in need of emergent operation as well as the utility of CT chest in asymptomatic elective surgical patients.

Introduction

Since December 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) has quickly become a global pandemic, drastically altering global way of life and clinical practices. Its high transmissibility rate, with a basic reproduction number (R_O) value estimated to be between 2-3, and its resultant rate of global spread are alarming (1,2). The overall mortality rate has been quoted to be between 2.3% to 7.3% (3,4).

Studies have demonstrated that patients who are older and those with increased comorbidities, including hypertension, diabetes, coronary artery disease, underlying respiratory condition, and obesity, are at a higher risk of adverse outcomes and mortality if infected with Coronavirus 2019 (COVID-19) (5,6). Estimates show that the in-hospital intubation rate is close to 20%, with roughly 80% of intubated patients ultimately dying, demonstrating an overall in hospital mortality rate of 16% (5–8). The perioperative morbidity and mortality associated with elective surgery is also higher among COVID-19 positive patients (5,8–10). In a recently published international study of 1,128 COVID-19 positive patients undergoing emergency (74.0%) and elective (24.8%) surgery, the overall 30-day mortality was 23.8%, with 51.2% of patients with a pulmonary complication (10). Of the patients who had a pulmonary complication, the mortality rate was 38.0% (10). Therefore, identifying COVID-19 positive patients prior to elective surgery and delaying non-emergent operations until patients recover from their acute infection will decrease potential morbidity and mortality in surgical patients.

Adequate testing, early diagnosis, isolation, and contact tracing have been the key to containing the spread of SARS-CoV2 (11). Currently, nasopharyngeal reverse transcriptase polymerase chain reaction (RT-PCR) is the most common way of testing for COVID-19. Problematic issues with these tests, however, include an approximately 30% false negative rate, results often taking many days to be reported, and the lack of availability of the tests themselves (12,13). However, characteristic findings on Computed Tomography Chest (CT Chest) scans may also serve as a means of diagnosis. CT scans typically demonstrate peripheral and subpleural lesions (96.1%), with ground glass opacities and consolidations (96.1%), and disease seen in all 5 lobes (74.5%) (14–16). Importantly, Pan et al. demonstrated that CT findings can change depending on the stage of SARS-CoV2 infection (17). Initially within the first 4 days of symptom onset, 75% of patients have characteristic findings of ground glass opacities, 25% "crazy-paving pattern", and 42% consolidation. As the infection progresses, repeat CT chest demonstrates further involvement in a bilateral multi-lobe distribution (5-8 days), increasingly prominent consolidation (9-13 days), and finally ground glass opacities with regression of crazy-paving pattern initially observed (>14 days after initial onset).

The aim of this paper was to examine available evidence that exists for evaluating CT chest as a diagnostic tool in comparison to the current standard of care, RT-PCR, for COVID-19 diagnosis for all symptomatic and asymptomatic patients. Clarifying the role and utility of CT Chest will be important as screening asymptomatic patients may lead to changes in the current screening algorithms for pre-surgical patients. Due to the high perioperative morbidity and mortality in COVID-19 positive patients, identifying COVID-19 patients accurately and quickly will be an important consideration prior to surgery.

Methods

A PRISMA compliant systematic review of the literature was conducted to evaluate available evidence regarding the sensitivity and general utility of CT chest in comparison to RT-PCR in COVID-19 diagnosis (18). A PRISM flowchart of the selection of relevant studies can be found in Figure 1. The PICO question formulated was: What is the sensitivity of CT Chest compared to RT-PCR for diagnosis of COVID-19 asymptomatic and symptomatic patients?

Search Strategy and Study Selection

Google Scholar® and MEDLINE®/PubMed® were used to search for primary articles evaluating the use of CT Chest for evaluation, screening, and diagnosis of COVID-19. Due to the limited data available and the fast-tracked publications accepted regarding COVID-19, some studies included are unpublished manuscripts or manuscripts submitted for publication. Studies from December 1, 2019 until June 7, 2020 were included. The MEDLINE®/PubMed® database was queried for the terms *CT chest, RT-PCR,* and *COVID 19.* Additionally, Google Scholar® was queried with the terms '*CT Chest'* and *'RT-PCR'* and *'COVID 19'* and *'sensitivity'*. All 90 results from MEDLINE®/PubMed® and the top 200 results from the Google Scholar® search were examined and studies that met inclusion criteria were included in the analysis.

Inclusion Criteria

The inclusion criteria for analysis of studies is as follows: 1) Study population of any patient (symptomatic and asymptomatic) undergoing testing for COVID-19 infection consisting of more than 5 patients. 2) Studies primarily using RT-PCR as a standard method of detecting COVID-19 infection, 3) Studies in which diagnostic CT Chest was performed in addition to RT-PCR, 4) Sensitivity and/or specificity of either study was recorded. Exclusion criteria consisted of eliminating case reports or series of 5 or less patients, studies dealing with other aspects of CT Chest in diagnosis of COVID-19 that did not specifically address comparison to RT-PCR.

Data Assessment and Determinization of Quality

Data was reviewed from the studies by the authors with type of study, total patient population, and sensitivities. The main outcome assessed in this review was an examination of the sensitivity of CT chest imaging in diagnosing COVID-19 infection in both symptomatic and asymptomatic COVID-19 positive patients compared to RT-PCR. Quality of the studies was judged based on the GRADE Working Group guidelines (19) and QUADAS 2 for diagnostic studies (20).

Results

Figure 1 represents a PRISMA flow chart demonstrating study selection and the studies that were ultimately included in our review (18). A total of 20 studies were identified that fit the inclusion criteria (Table 1 & 2). The studies examined were grouped by patient symptoms in relation to diagnostic testing with RT-PCR and CT Chest.

COVID-19 Symptomatic Patients

There were 17 primary studies found in the literature that assessed the sensitivity of CT Chest compared to RT-PCR in symptomatic COVID-19 positive patients with sensitivities ranging from 57% to 100% depending on the study (Table 1). An examination of these studies demonstrated that 15 studies were retrospective analyses with only 2 prospective studies identified.

The retrospective studies examined demonstrated a high sensitivity rate for CT Chest in comparison to RT-PCR in symptomatic COVID-19 patients (15–17,21–32). The largest study to date, by Ai et al., is a retrospective analysis which included 1,014 patients who were being tested for COVID-19 in Wuhan, China (26). The study directly compared the efficacy of CT chest with RT-PCR for diagnosis of suspected COVID-19 patients presenting with clinical symptoms, such as fever and cough (26). RT-PCR identified 59% of COVID-19 patients, while CT chest detected 88% of positive patients (26). The sensitivity of CT chest was 97 % (95% CI, 95-98%) based on positive RT-PCR results (26). In patients who were RT-PCR negative, 75% of these patients had CT scan findings consistent with positive COVID-19 results. For RT-PCR negative patients, patients were classified into highly likely, probable or uncertain based on follow up CT scans. Mean result time for RT-PCR to turn from negative to positive was 5.1±1.5 days, while CT scan results were more immediate with a higher sensitivity than RT-PCR (26). Specificity, however, was quoted to be 25% (95%CI, 22-30%) in this study (26).

The importance of early timing of CT Chest along with RT-PCR was continually emphasized in the studies reviewed as CT Chest had a higher sensitvity in symptomatic COVID-19 patients with negative RT-PCR early on in the infection course (27,28). Fang et al. found a similar lead time to Ai et al. in a retrospective review of 51 patients (26,27). In this study, patients were included who either had travelled to high-risk areas and contact with those with symptoms or were themselves symptomatic (27). Ninety-eight percent (95% CI 90-100%) of patients with COVID-19 had evidence of abnormal CT findings at an average of 3±3 days from initial onset of disease, while RT-PCR testing has been demonstrated to be only 71% (95% CI 56-83%) sensitive at 3±3 days ($p<0.001$) (27). Sensitivity of RT-PCR increased as sequential tests were done after initial testing—with 23.5% of patients requiring a 2nd test, 3.9% requiring a 3rd test, and 2.0% requiring a 4th test (27). Pan et al. demonstrated that > 75% of RT-PCR positive patients, displayed characteristic findings on CT within the first four days; in this study, however, they found the peak of findings on CT chest to occur 10 days after the onset of symptoms (17).

The two prospective studies included in this review were by Caruso et al. and Giemeta et al (33,34). Caruso et al., enrolled 158 consecutive patients suspected to have COVID-19 infection based on symptoms of fever, cough and dyspnea (33). All patients underwent RT-PCR and chest CT to assess for infection, with 39% of patients being positive for RT-PCR, and 64% of patients with positive CT findings. These included ground glass opacities (100%), multilobe involvement (93%), and bilateral pneumonia (91%) (33). Overall sensitivity, specificity, and accuracy of CT scan for COVID-19 pneumonia were 97% (95% IC, 88-99%), 56% (95% IC, 45-66%) and 72% (95% IC 64-78%), respectively (33). Giemeta et al. enrolled patients over a 10-day period that presented to the Emergency Department with symptoms characteristic of COVID-19 (34). Patients were tested with both RT-PCR and CT. CT was shown to have a sensitivity of 89.2% and was more likely to be predictive in those who were at high risk for pneumonia and with sepsis (34).

Specificity was examined by some, but not all of the studies that were included in this analysis. The specificity reported varied widely by study and ranged from 24-100% (26,35). In Bai et al., seven radiologists blindly reviewed the scans of 219 patients with a diagnosis of "pneumonia", with the following results: a median specificity of 93%, with three of the radiologists demonstrating 100% specificity; the sensitivity in the same study ranged from 67-97% (35). Another study from Japan by Himoto et al. of clinically symptomatic patients reported specificity of 93% (95% CI of 67%-98%) when taking more specific CT scan characteristics into account, such as bilateral ground glass opacities, and peripheral predominant lesions without airway abnormalities, nodules, mediastinal lymphadenopathy or pleural effusions (30).

COVID-19 Asymptomatic Patients

Our systematic review identified 3 articles that met our inclusion criteria and compared the sensitivity of CT Chest to RT-PCR in asymptomatic COVID-19 positive patients (Table 2) (36–38). The largest cohort of asymptomatic patients in this review comes from Inui et al (36). Inui et al looked at 104 confirmed RT-PCR cases from the Diamond Princess Cruise Ship (36). In this study, 76 of the patients were asymptomatic and 41 patients were symptomatic (36). The asymptomatic patients were less likely than the symptomatic patients to have abnormal findings on CT scan, with 54% having characteristic CT findings in the asymptomatic group and 79% having CT findings in the symptomatic group (36). Another retrospective analysis identified 63 asymptomatic, RT-PCR confirmed, COVID-19 positive patients through contact tracing with COVID-19 positive individuals (37). Of the asymptomatic patients who underwent CT chest, 46% had abnormal CT chest findings (37). In contrast, Shi et al. found that 15 of 15 asymptomatic, but RT-PCR positive patients in Wuhan, China displayed ground glass opacities on CT chest (38).

Discussion

Knowledge of diagnosis and treatment modalities of COVID-19 is a rapidly evolving landscape as new information is obtained about the infection on a weekly basis. The advantage of CT scan to detect COVID-19 in symptomatic patients with a higher sensitivity and at an earlier time period of infection is important and should be further clarified in prospective studies (17,39–41). The potential implications of using CT scan as an adjunct for diagnosis and assessment of disease progression in symptomatic patients can be important in the diagnosis of RT-PCR negative patients with COVID-19 symptoms who require emergency or urgent surgery. Based on current evidence, CT scans have been shown to have a higher sensitivity early in the infectious time course for symptomatic patients in comparison to conventional RT-PCR, but its utility continues to remain uncertain in asymptomatic patients, especially regarding preoperative surgical patients. Identifying the role of CT imaging in diagnosis of COVID-19 in symptomatic and asymptomatic patients can be important as it is a readily available tool in nearly all healthcare facilities in the world, and the results are immediately reported.

There appears to be a role for CT imaging beyond simply that of a resource constrained environment as recently suggested by a Multinational Consensus from the Fleischner Society (42). Given the high perioperative morbidity and mortality seen in several reviews of COVID-19 patients undergoing surgery, even elective surgery (5,8–10), and the increased rate of transmission to healthcare providers during aerosolized procedures, a CT chest can be a useful pre-procedural diagnostic adjunct to surgeons, endoscopists, anesthesiologists, and other procedural personnel prior to any aerosolizing procedures (16,43–46). With this information, it may be recommended that for a patient with any clinical symptoms of COVID-19 should potentially undergo a CT chest in addition to RT-PCR and typical CT abdomen/pelvis required prior to certain procedures (cancer, urgent or emergent abdominal operation, endoscopy, etc.). This will lead to the operations being performed in a timely fashion for those without findings on CT chest and decrease the overall hospital stay and cost. This rationale appears consistent with The Royal College of Radiologists recent recommendations that patients who are suspected to have an abdominal emergency should undergo concurrent CT chest at the time of CT abdomen/pelvis (47).

CT chest protocols are varied between studies, but intravenous contrast medium is not necessary to make a diagnosis (27,33). The radiation doses needed for adequate detection of COVID-19 were not recorded in many studies (16,26,27,33), but the average CT dose index (CTDIvol) was 8.4 ± 2.0 mGy (range 5.2-12.6 mGy) for examining COVID-19 patients (17) It is suggested that reducing a patient's radiation dose to 1/8 or 1/9 of the standard dose (0.203 mSv) will still allow for adequate imaging of lung parenchyma to identify SARS-CoV2 infection (44). Each standard dose CT scan (4-7 mSv) confers an oncological risk of 0.05-0.7%; by further decreasing that risk 8 to 9 fold, the potential benefits far outweigh the potential adverse effect to patients (44,48,49).

Interestingly, CT scans can accurately predict not only a positive COVID-19 infection in symptomatic patients, but also potentially assess the stage of infection and the time point and duration of infection (15,17). While RT-PCR provides a qualitative answer, CT scans may allow clinicians a glimpse of the duration of infection with different findings at each stage (17). While more information regarding the patterns of CT scans during the time course of infection is needed, this provides a context for a positive COVID-19 test. CT chest can actually help clinicians to delineate the progression of the infective process in a patient, which could provide an optimal time frame for when an operation or procedure can safely be performed in patients requiring emergent or urgent operations. Given the high perioperative morbidity and mortality known thus far in COVID-19 positive patients, elective operations should be deferred in COVID-19 positive patients regardless of symptoms (5,8–10).

The role of using pre-operative CT scan is certainly less clear in asymptomatic patients (36,38,40,50). The evidence suggest that there is less utility for CT scan in asymptomatic patients compared to symptomatic patients (36,38,40,50). There is also relatively little evidence available specifically addressing management in asymptomatic presurgical patients. A meta-analysis performed by Kim et. al demonstrated that the prevalence of disease also seemed to play a role in positive predictive value (PPV), with only 14.2% PPV at a prevalence of 10%, compared to a 90.8% PPV compared to RT-PCR (41). Additionally, they found that sensitivity is affected by the proportion of asymptomatic patients included, and that in low prevalence countries, the positive predictive value of CT scan was ten times lower than that of RT_PCR (41). Whether or not CT chest will have any further value in addition to RT-PCR in asymptomatic patients in preoperative (abdominal surgery) patients specifically is yet to be determined, and there should be caution extrapolating data from symptomatic patients to asymptomatic patients.

Clinical trials evaluating the role of CT chest in asymptomatic patients are underway in the Netherlands with formal results still pending (50). Preliminary results of this prospective study from the Netherlands screening asymptomatic patients preoperatively using both CT Chest and RT-PCR prior to elective procedures demonstrated a total of 1.5%-2.0% COVID-19 positive patients (50). In this study, CT Chest afforded an additional value of 0.1% in identifying patients that RT-PCR potentially missed (50). Final results from this study will be helpful in identifying if screening asymptomatic patients with CT Chest preoperatively is necessary. Until more evidence is available in this rapidly changing landscape, it will remain unclear what the role of CT Chest will be as a general screening tool for COVID-19 infection in preoperative (abdominal surgery) patients.

The main limitation of this study is the quality of the evidence currently available. At this time, because of the retrospective nature of most of the studies regarding CT chest and RT-PCR, there is a high selection bias. Almost all of the studies conducted thus far have been conducted in symptomatic patients with a few studies examining just asymptomatic patients. The overall GRADE of the recommendations of the papers reviewed is low, as most of the studies in this review consist of retrospective analyses (19). Additional use of the QUADAS 2 Assessment further demonstrates that there is a high risk for potential bias due to study design and patient selection. The concern regarding applicability of the evidence available thus far is low (Table 3 & Figure 2). Further investigation regarding perioperative screening protocols, in asymptomatic and symptomatic patients, along with better-defined radiological criteria for detecting COVID-19 and its progression is still needed.

Conclusion

CT chest can be a highly sensitive diagnostic test for any symptomatic COVID-19 positive patients and is capable of detecting COVID-19 infection earlier in the infectious course than RT-PCR. Based on preliminary findings, CT chest should be considered along with CT abdomen & pelvis in symptomatic presurgical patients who require accurate and fast diagnosis in clinical settings where RT-PCR is not readily available or has a long turnaround time (i.e. those who may need emergency laparotomy for an acute intraabdominal process). In asymptomatic presurgical patients (i.e. elective abdominal surgery patients), there is currently insufficient evidence to recommend routine preoperative CT Chest. Further study is needed to make definitive recommendations.

Acknowledgements

None

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Table 1 – Primary Studies: COVID-19 Symptomatic Patients

Study/Country	Type of Study	N	Mean Age (in years) ± SD	Gender (M)	Reported Sensitivity of CT Chest (CI if available)
Ai et al., China	Retrospective	1014	51 ± 15 years	46%	97 % (95%CI, 95-98%)
Bai et al., China/USA	Retrospective	219	44.8 ± 14.5	54%	67-94%
Bernheim et al., China	Retrospective	121	45.3	50%	88%, as measured "late" in disease
Caruso et al. Italy	Prospective	158	57 ± 15	52%	97% (95% IC, 88-99%)
Chen et al., China	Retrospective	21	49 ± 15.7	57%	95%
Dangis et al., Belgium	Retrospective	192	61 ± 18.2	45%	86.7%
Fang et al., China	Retrospective	51	45	57%	98%, (95% CI 90-100%)
Fu et al., China	Retrospective	64	46.1 ± 13.1	45%	85.9%
Gietema et al., Netherlands	Prospective	193	66	58%	89.2%
He et al., China	Retrospective	82	52	50%	79%
Himoto et al., Japan	Retrospective	21	58.5	57%	100%
Li et al., China	Retrospective	225	50 ± 14	53%	86.2%
Miao et al., China	Retrospective	130	45.1 ± 13.4	52%	57%
Pan et al., China	Retrospective	84	40 ± 9	29%	100% when all time periods measured
Wang K et al., China	Retrospective	114	53	49%	96.5%
Wen et al., China	Retrospective	103	46	46%	93% (95% CI: 85-97%)
Zhao et al., China	Retrospective	34	48	58%	89.5%

Table 2 – Primary Studies: COVID-19 Asymptomatic Patients

Study/Country	Type of Study	N	Mean Age (in years) ± SD	Gender (M)	Reported Sensitivity for CT Chest (Positive Tests)
Inui et al., Japan	Retrospective	104	62 ± 16	58%	60.6%
Shi et al. China	Retrospective	81	49.5	58%	100%
Wang Y et al., China	Retrospective	63	39.3 ± 16.5	54%	46%

Table 3 – Assessment of Quality of Evidence using GRADE and QUADAS 2 Tool

	STUDY	GRADE*	QUADAS 2†						
			Risk of Bias				*Applicability Concerns*		
			Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Symptomatic COVID-19 Patient Studies	Ai et al.	Low	High	High	High	High	Low	Low	Low
	Bai et al.	Low	High	High	High	High	Low	Low	Low
	Bernheim et al.	Very Low	Low	High	Low	Low	Low	Low	Low
	Caruso et al.	Moderate	Low	Low	Low	Low	Low	Low	Low
	Chen et al.	Low	High	Low	Unclear	Low	Low	Low	Low
	Dangis et al.	Low	High	Unclear	Unclear	Unclear	Low	Low	Low
	Fang et al.	Low	Low	Unclear	Low	High	Low	Low	Low
	Fu et al.	Low	High	High	Low	Unclear	Low	Low	Low
	Gietema et al.	Moderate	Low	Low	Low	Low	Low	Low	Low
	He et al.	Very low	Low	Low	Low	Low	Low	Low	Low
	Himoto et al.	Very low	High	Low	Unclear	Unclear	Low	Low	Low
	Li et al.	Low	Unclear	Unclear	Low	Unclear	Low	Low	Low
	Miao et al.	Low	Low	Low	Low	Unclear	Low	Low	Low
	Pan et al.	Low	High	Unclear	Low	Unclear	High	Low	Low
	Wang K et al.	Low	Low	Low	Low	Low	Low	Low	Low
	Wen et al.	Low	Low	Low	Low	Unclear	Low	Low	Low
	Zhao et al.	Very low	Low	Low	Low	Unclear	Low	Low	Low
Asymptomatic	Inui et al.	Low	High	Low	Low	Low	High	Low	Low

COVID-19 Patient Studies	**Shi et al.**	Low	High	High	Low	High	Low	Low	Low
	Wang Y et al.	Low	High	Unclear	Low	Unclear	High	Low	Low

* Oxman et al. *British Medical Journal. BMJ Publishing Group*; 2004. p. 1490–4.

† QUADAS-2 | Bristol Medical School: Population Health Sciences

Figure 1: PRISMA Flowchart

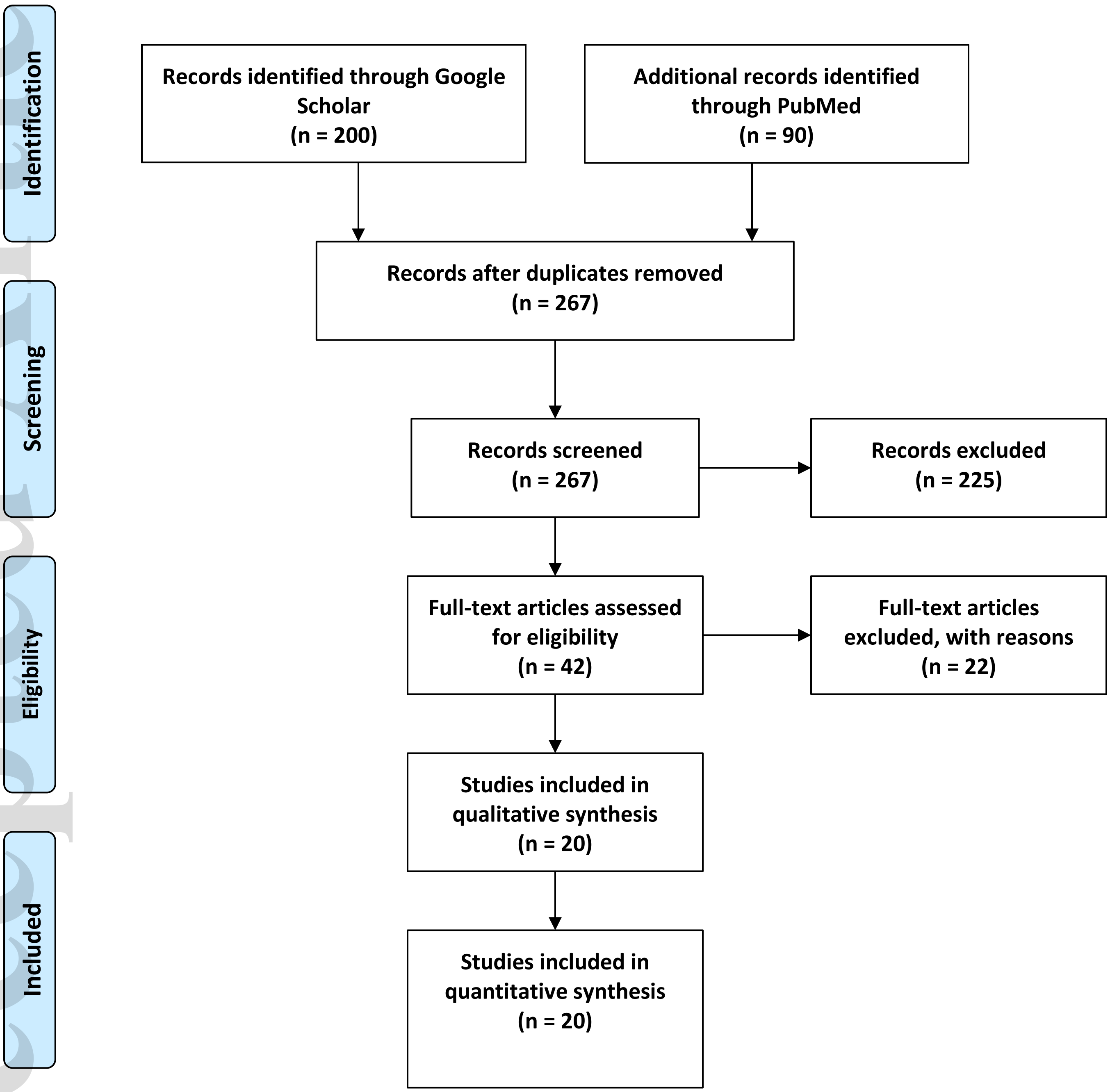

Figure 2: QUADAS 2 Assessment